

FIG. 1

Mature Human GDNF

TCA	CCA	GAT	AAA	CAA	ATG	GCA	GTG	CTT	CCT	AGA	AGA	GAG	CGG	AAT	5	10	15
Ser	Pro	Asp	Lys	Gln	Met	Ala	Val	Leu	Pro	Arg	Arg	Glu	Arg	Asn			
CGG	CAG	GCT	GCA	GCT	GCC	AAC	CCA	GAG	AAT	TCC	AGA	GGA	AAA	GGT	20	25	30
Arg	Gln	Ala	Ala	Ala	Ala	Asn	Pro	Glu	Asn	Ser	Arg	Gly	Lys	Gly			
CGG	AGA	GGC	CAG	AGG	GGC	AAA	AAC	CGG	GGT	TGT	GTC	TTA	ACT	GCA	35	40	45
Arg	Arg	Gly	Gln	Arg	Gly	Lys	Asn	Arg	Gly	Cys	Val	Leu	Thr	Ala			
ATA	CAT	TTA	AAT	GTC	ACT	GAC	TTG	GGT	CTG	GGC	TAT	GAA	ACC	AAG	50	55	60
Ile	His	Leu	Asn	Val	Thr	Asp	Leu	Gly	Leu	Gly	Tyr	Glu	Thr	Lys			
GAG	GAA	CTG	ATT	TTT	AGG	TAC	TGC	AGC	GGC	TCT	TGC	GAT	GCA	GCT	65	70	75
Glu	Glu	Leu	Ile	Phe	Arg	Tyr	Cys	Ser	Gly	Ser	Cys	Asp	Ala	Ala			
GAG	ACA	ACG	TAC	GAC	AAA	ATA	TTG	AAA	AAC	TTA	TCC	AGA	AAT	AGA	80	85	90
Glu	Thr	Thr	Tyr	Asp	Lys	Ile	Leu	Lys	Asn	Leu	Ser	Arg	Asn	Arg			
AGG	CTG	GTG	AGT	GAC	AAA	GTA	GGG	CAG	GCA	TGT	TGC	AGA	CCC	ATC	95	100	105
Arg	Leu	Val	Ser	Asp	Lys	Val	Gly	Gln	Ala	Cys	Cys	Arg	Pro	Ile			
GCC	TTT	GAT	GAT	GAC	CTG	TCG	TTT	TTA	GAT	GAT	AAC	CTG	GTT	TAC	110	115	120
Ala	Phe	Asp	Asp	Asp	Leu	Ser	Phe	Leu	Asp	Asp	Asn	Leu	Val	Tyr			
CAT	ATT	CTA	AGA	AAG	CAT	TCC	GCT	AAA	AGG	TGT	GGA	TGT	ATC		125	130	
His	Ile	Leu	Arg	Lys	His	Ser	Ala	Lys	Arg	Cys	Gly	Cys	Ile				

FIG. 2

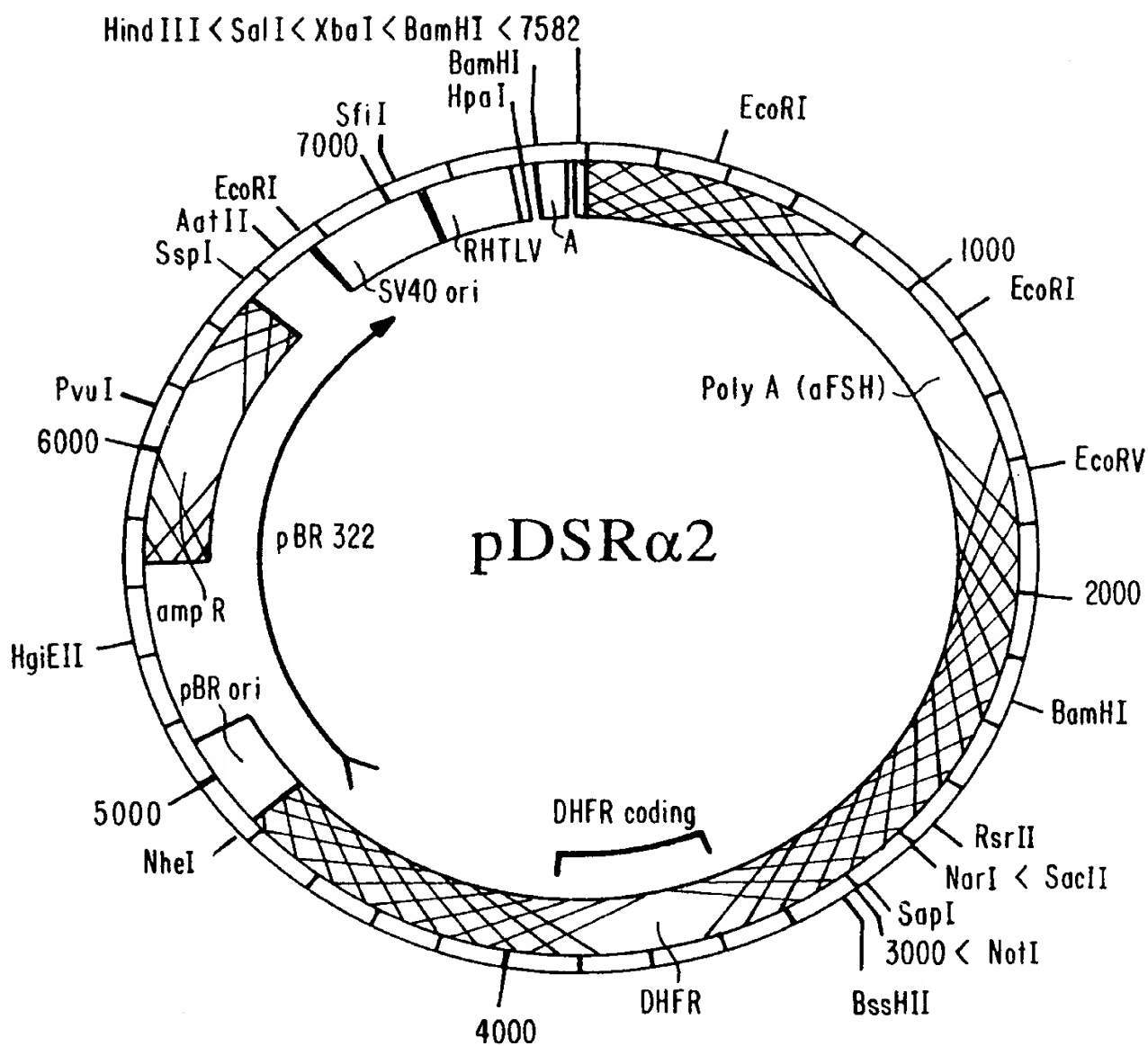


FIG.3B

S
u
n
I

241 CCTGCGACGCTGCTGAAACCACGTACGACAAAATCCTGAAAAACCTGTCCCGTAACCGTC 300

H i n d I P v u I

301 GTCTGGTTTCCGACAAAGTTGGTCAAGCTTGCTGCCGTCCGATCGCTTTCGACGACGACC 360

361 TGCCTTCCTGGACGACAACCTGGTTTACCACATCCTGCGTAAACACTCCGCTAAGCGTT 420

B
a
m
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421 GCGGTTGCATCTAAGGATCC 440

FIG.4

metGDNF Degenerate DNA Sequence

N
d
e
I
CATATGAGCCCGGACAAACAG
 1 -----+-----+-----+-----+-----+-----+ 60
 MetSer
 ATGGCAGTACTTCCACGTCGTGAACGTAATCGCCAGGCAGCAGCTGCAAACCCGGAAAAC
 61 -----+-----+-----+-----+-----+-----+ 120
 TCCCGTGGTAAAGGTCGCCGTGGCCAGCGCGGCAAAAACCGTGGTTGTGTTCTGACTGCA
 121 -----+-----+-----+-----+-----+-----+ 180
 P
s
h
A
I
ATCCACCTGAACGTTACTGACCTGGGTCTGGGCTACGAAACCAAAGAAGAACTGATCTTC
 181 -----+-----+-----+-----+-----+-----+ 240
 P
s
t
I
CGCTACTGCAGCGGCTCTTGCGACGCAGCTGAAACCACTTACGACAAAATCCTGAAAAAC
 241 -----+-----+-----+-----+-----+-----+ 300
 P
v
u
I
CTGTCCCGTAACCGCCGTCTGGTAAGCGACAAAGTAGGTCAGGCATGCTGCCGTCCGATC
 301 -----+-----+-----+-----+-----+-----+ 360
 B
s
m
I
GCATTCGACGATGACCTGAGCTTCCTGGATGACAACCTGGTTTACCACATCCTGCGTAAA
 361 -----+-----+-----+-----+-----+-----+ 420
 B
a
m
H
I
CACTCCGCTAAACGCTGCGGTTGCATCTAAGGATCC
 421 -----+-----+-----+-----+-----+ 456

FIG.5

[Pro²³-Lys³⁷ΔAsn³⁷-Ile¹³⁴] Truncated GDNF Protein

ATGTCCCCAGAAAATTCTCGTGGTAAAGGTCGTCGTGGTCAGCGTGGTAATAACCGCGGT
21 -----+-----+-----+-----+-----+-----+ 80
M S P E N S R G K G R R G Q R G N N R G
TGCGTTCTGACCGCTATCCACCTGAACGTTACCGACCTGGGTCTCGGTTACGAAACCAAA
81 -----+-----+-----+-----+-----+ 140
C V L T A I H L N V T D L G L G Y E T K
GAAGAATTAATCTTCCGTTACTGCTCCGGTTCCTGCGACGCTGCTGAAACCACGTACGAC
141 -----+-----+-----+-----+-----+ 200
E E L I F R Y C S G S C D A A E T T Y D
AAAATCCTGAAAAACCTGTCCCGTAACCGTCGTCTGGTTTCCGACAAAGTTGGTCAAGCT
201 -----+-----+-----+-----+-----+ 260
K I L K N L S R N R R L V S D K V G Q A
TGCTGCCGTCCGATCGCTTTCGACGACGACCTGTCCTTCCTGGACGACAACCTGGTTTAC
261 -----+-----+-----+-----+-----+ 320
C C R P I A F D D D L S F L D D N L V Y
CACATCCTGCGTAAACACTCCGCTAAGCGTTGCGGTTGCATCTAA
321 -----+-----+-----+-----+-----
H I L R K H S A K R C G C I *

FIG.6

[Arg³²-Ile¹³⁴] Truncated GDNF Protein

ATGCGTGGTCAACGTGGTAAAAACCGCGGTTGCGTTCTGACTGCAATCCACCTGAACGTT
41 -----+-----+-----+-----+-----+-----+ 100
M R G Q R G K N R G C V L T A I H L N V

ACTGACCTGGGTCTGGGCTACGAAACCAAAGAAGAACTGATCTTCCGCTACTGCAGCGGC
101 -----+-----+-----+-----+-----+-----+ 160
T D L G L G Y E T K E E L I F R Y C S G

TCTTGCGACGCAGCTGAAACCACTTACGACAAAATCCTGAAAAACCTGTCCCGTAACCGC
161 -----+-----+-----+-----+-----+-----+ 220
S C D A A E T T Y D K I L K N L S R N R

CGTCTGGTAAGCGACAAAGTAGGTCAGGCATGCTGCCGTCCGATCGCATTCGACGATGAC
221 -----+-----+-----+-----+-----+-----+ 280
R L V S D K V G Q A C C R P I A F D D D

CTGAGCTTCCTGGATGACAACCTGGTTTACCACATCCTGCGTAAACACTCCGCTAAACGC
281 -----+-----+-----+-----+-----+-----+ 340
L S F L D D N L V Y H I L R K H S A K R

TGCGGTTGCATCTAA
341 -----+----- 355
C G C I *

FIG.7

[Gly³³-Ile¹³⁴] Truncated GDNF Protein

ATGGGTCAACGTGGTAAAAACCGTGGTTGTGTTCTGACTGCAATCCACCTGAACGTTACT
41 -----+-----+-----+-----+-----+-----+ 100
M G Q R G K N R G C V L T A I H L N V T

GACCTGGGTCTGGGCTACGAAACCAAAGAAGAACTGATCTTCCGCTACTGCAGCGGCTCT
101 -----+-----+-----+-----+-----+-----+ 160
D L G L G Y E T K E E L I F R Y C S G S

TGCGACGCAGCTGAAACCACTTACGACAAAATCCTGAAAAACCTGTCCCGTAACCGCCGT
161 -----+-----+-----+-----+-----+-----+ 220
C D A A E T T Y D K I L K N L S R N R R

CTGGTAAGCGACAAAGTAGGTCAGGCATGCTGCCGTCCGATCGCATTTCGACGATGACCTG
221 -----+-----+-----+-----+-----+-----+ 280
L V S D K V G Q A C C R P I A F D D D L

AGCTTCCTGGATGACAACCTGGTTTACCACATCCTGCGTAAACACTCCGCTAAACGCTGC
281 -----+-----+-----+-----+-----+-----+ 340
S F L D D N L V Y H I L R K H S A K R C

GGTTGCATCTAA
341 -----+--- 352
G C I *

FIG.8

Comparison of Protein Sequences

						50
	GDNF	MSPDKQMAVL	PRRERNRQAA	AANPENSRGK	GRRGQRGKNR	GCVLTAIHLN
-31	GDNFMRGQRGKNR	GCVLTAIHLN
-32	GDNFMGQRGKNR	GCVLTAIHLN
-22	GDNFMSPENSRGK	GRRGQRGNR	GCVLTAIHLN
		51				100
	GDNF	VTDLGLGYET	KEELIFRYCS	GSCDAAETTY	DKILKNLSRN	RRLVSDKVGQ
-31	GDNF	VTDLGLGYET	KEELIFRYCS	GSCDAAETTY	DKILKNLSRN	RRLVSDKVGQ
-32	GDNF	VTDLGLGYET	KEELIFRYCS	GSCDAAETTY	DKILKNLSRN	RRLVSDKVGQ
-22	GDNF	VTDLGLGYET	KEELIFRYCS	GSCDAAETTY	DKILKNLSRN	RRLVSDKVGQ
		101			135	
	GDNF	ACCRPIAFDD	DLSFLDDNLV	YHILRKHSK	RCGCI	
-31	GDNF	ACCRPIAFDD	DLSFLDDNLV	YHILRKHSK	RCGCI	
-32	GDNF	ACCRPIAFDD	DLSFLDDNLV	YHILRKHSK	RCGCI	
-22	GDNF	ACCRPIAFDD	DLSFLDDNLV	YHILRKHSK	RCGCI	